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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/527,438

03/11/2005

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06/01/2007

NATH & ASSOCIATES

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EXAMINER

JOIKE, MICHELE K

ART UNIT

PAPER NUMBER

1636

MAIL DATE

DELIVERY MODE

06/01/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/527,438	Applicant(s) CHOI ET AL.	
	Examiner Michele K. Joike, Ph.D.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 March 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>3/11/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-33 are pending and examined.

Priority

Applicant is advised of possible benefits under 35 U.S.C. 119(a)-(d), wherein an application for patent filed in the United States may be entitled to the benefit of the filing date of a prior application filed in a foreign country.

Receipt is acknowledged of Korean application 10-2002-0055575 filed on September 13, 2002 and submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. It is noted that no English translation has been filed.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Figure 2 contains amino acid sequences that need sequence identifiers.

Claim Objections

Claim 1 is objected to because of the following informalities: "the mutant lipase displayed in the surface" (lines 11-12) should be "the mutant lipase displayed on the surface". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the transformants are required to practice the invention. As such, the transformants must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the transformants. In the instant case, the process to generate the transformants that is disclosed in the specification does not appear to be repeatable, nor does it appear the transformants are readily available to the public.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a

Art Unit: 1636

- patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:
- a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;
 - b) all restrictions upon availability to the public will be irrevocably removed upon the granting of the patent;
 - c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request for the enforceable life of the patent, whichever is longer;
 - d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and
 - e) the deposit will be replaced if it should ever become inviable.

Failure to make one of the preceding indications in response to this Office Action will result in the rejection being maintained in either a second Non-Final or a Final rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the surface display vector fragment" in line 9.

There is insufficient antecedent basis for this limitation in the claim.

Art Unit: 1636

Furthermore, it is unclear why a vector fragment is being introduced into the cell, since there is no indication that it is being used or performing any function. For purposes of examination, the Examiner is assuming that fragment can mean the entire vector.

Also, in claim 1, it is unclear what "evolved activity" means, in the last line. There is no definition in the specification. If Applicant meant improved activity, the Examiner suggests that term be used instead.

Regarding claim 8, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

In claims 28 and 29, an accession number is recited at the end of the claim. It is unclear to what the accession number is referring. Is the accession number for the transformant with a gene comprising SEQ ID NO: 6 (claim 28) or 7 (claim 29), or with one the mutations listed? If it is the latter, which mutation is it?

The term "proper" in claim 31 is a relative term which renders the claim indefinite. The term "proper" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Since no specific host cell or organism is designated, it is unclear how a proper temperature can be determined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claims 1, 3-6 and 8, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,020,180 in view of Kim et al.

Applicants claim a method for screening of a mutant lipase having an improved enzymatic activity comprising the following steps: 1) Cloning a lipase gene into a surface display vector; 2) Preparing a mutant lipase gene library by mutagenic PCR using the lipase gene in the surface display vector of the step 1 as a template; 3)

Art Unit: 1636

Transforming the mutant lipase gene library of the step 2 and the surface display vector fragment into host cells; and 4) Measuring the activity of the mutant lipase displayed in the surface of the transformed host cell and selecting the lipase showing evolved activity. The host cell is a yeast cell from the *Hansenula* or *Saccharomyces* genus. The vector includes a MOX or GAPDH promoter, an α -amylase signal sequence, a CWP1, GAS1 or TIP1 surface display mediating gene, and a terminator.

US 6,020,180 (specifically col. 1, 3, 10-12 and 14) teaches a method for identifying lipase variants with improved properties. The lipase used is *Candida antarctica* lipase A. Recombinant expression vectors carrying a promoter, terminator, secretion signal (α -amylase), and the gene encoding the mutant lipase is transformed into a host cell. Host cells used include *Hansenula* and *Saccharomyces*. The lipase variant is produced by culturing the cells, wherein the mature lipase is secreted from the cell, and then the lipase variant is recovered from the culture. The DNA sequences encoding the lipase may be mutated using site-directed mutagenesis. More than one lipase variant is created using site-directed mutagenesis, there a library is made and used. The specific activity of the mutant lipases is determined. Improved properties means that the lipase variant has increased specific activity as compared to the parent enzyme.

However, it does not teach a CWP1, GAS1 or TIP1 surface display mediating gene, or a surface display vector. It also does not teach a MOX or GAPDH promoter.

Kim et al (Yeast, 19: 1153-1163, 2002, specifically materials & methods and p. 1154) teach a cell surface display system using anchored proteins in *Hansenula*. The

Art Unit: 1636

cell surface display vector includes a MOX or GAPDH promoter, an α -amylase signal sequence, and a CWP1, GAS1 or TIP1 surface display mediating gene.

The ordinary skilled artisan, desiring to use cell surface display vector including a MOX or GAPDH promoter, an α -amylase signal sequence, and a CWP1, GAS1 or TIP1 surface display mediating gene in a method for screening of a mutant lipase having an improved enzymatic activity, would have been motivated to combine the teachings of US 6,020,180 on a method for identifying lipase variants with improved properties, as described above, with Kim et al who teach a cell surface display vector including a MOX or GAPDH promoter, an α -amylase signal sequence, and a CWP1, GAS1 or TIP1 surface display mediating gene, because Kim et al state that a surface display system in *Hansenula* can provide a valuable tool for a screening system for useful protein ligands. It would have been obvious to one of ordinary skill in the art to use the cell surface display system because the screening system is useful for design of various biocatalysts to perform bioprocesses. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,020,180 in view of Kim et al and in further view of Uppenberg et al.

Applicants claim the lipase gene as a *Candida antarctica* lipase B gene, represented by SEQ ID NO: 14.

Art Unit: 1636

US 6,020,180 teaches all of the limitations as described above. However, it does not teach the use of *Candida antarctica* lipase B.

Kim et al teach all of the limitations as described above. However, they do not teach the use of *Candida antarctica* lipase B.

Uppenberg et al (Structure 2(4): 293-308, 1994, specifically pp. 293, 303 and Figure 1) teach the use of *Candida antarctica* lipase B cloned into a vector, transformed into *E. coli*, and then screened. The sequence in Figure 1 contains SEQ ID NO:14, with an additional DNA sequence on the 5' end encoding a signal peptide. Since "represented" is treated as open language, the sequence in Figure 1 reads on SEQ ID NO: 14.

The ordinary skilled artisan, desiring to use the *Candida antarctica* lipase B gene, would have been motivated to combine the teachings of US 6,020,180 on a method for identifying lipase variants with improved properties, as described above, with Kim et al who teach a cell surface display vector including a MOX or GAPDH promoter, an α -amylase signal sequence, and a CWP1, GAS1 or TIP1 surface display mediating gene, with Uppenberg et al teaching the *Candida antarctica* lipase B gene, because Uppenberg et al state that *Candida antarctica* lipase B is of particular interest because it displays strong stereospecificity on chiral substrates during hydrolysis or organic synthesis. It would have been obvious to one of ordinary skill in the art to use *Candida antarctica* lipase B because of its ability to hydrolyze triglycerides at an oil-water interface. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the

Art Unit: 1636

contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

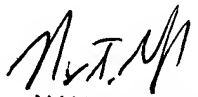
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1636

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele K Joike, Ph.D.
Examiner
Art Unit 1636


NANCY VOGEL
PRIMARY EXAMINER